REMARKS

Reconsideration of the Final Office Action mailed September 26, 2002, (hereinafter "instant Office Action"), entry of the foregoing amendments and withdrawal of the rejection of claims 1-88, are respectfully requested.

In the instant Office Action, claims 1-88 are listed as pending, and claims 1-88 are listed as rejected.

Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendments. Appendix A is captioned **"Version with markings to show changes made"**. Applicants would like to point out that in the Reply mailed August 26, 2002, Appendix A inadvertently contained the wrong formula in Claim 1. However, the formula in Claim 1 on page 2 of the Reply mailed August 26, 2002 was correct.

The Examiner has rejected claims 1-88 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection. Applicants response to the Examiner's enumerated points are numbered accordingly to track the Examiner's points.

i) With respect to the term "prodrug", Applicants maintain the arguments presented in the last Reply which was filed August 26, 2002. Applicants assert that "prodrug" is a term of art that is well understood by those skilled in the art. In this regard, the Examiner's attention is invited to Chapter 8, entitled "Prodrugs and Drug Delivery Systems," in The Organic Chemistry of Drug Design and Drug Action, by Richard Silverman, © 1992 Academic Press, San Diego (hereinafter "Silverman"). A copy of Chapter 8 is enclosed for the Examiner's convenience as Exhibit 1. A prodrug is a pharmacologically inactive compound that is converted to an active drug, i.e., one of the compounds of the present invention, by a metabolic transformation (p. 352 of Silverman). Prodrugs may be synthesized from, *inter alia*, alcohols, carboxylic acids, and amines using art-recognized techniques, such as those summarized in Silverman pp. 355 – 388. Regardless of the core structure to which the alcohol, carboxylic acid or amine group is attached, these moieties act in such a way as to form prodrugs. An example of

Applicants' compounds as an alcohol is when R_2 is B-E and B is hydroxy. Applicants' compound is a carboxylic acid when Z_{110} is COOH . Applicants' compound is an amine when R_3 is H. Accordingly, Applicants assert that one of ordinary skill in the art would be able to make and use prodrugs of the present invention without undue experimentation using well-known, art-recognized techniques such as those disclosed in Chapter 8 of the Silverman reference. Additionally, the term "prodrug" is analogous to the term "pharmaceutically acceptable salt" in that its meaning is understood by those skilled in the art. The term "pharmaceutically acceptable salt" has been accepted by the examiner.

With respect to the phrase "or biologically active metabolites", Applicants have amended claims 1, 33, 35, 36, 38, 40, 45, 46, and 48 to delete the phrase "or biologically active metabolites".

ii) With respect to the term "substituted", Applicants maintain the arguments presented in the last Reply which was filed August 26, 2002. In addition, Applicants have provided a representative list of suitable substituents on page 55, lines 19-24 of the instant specification. From this list, one skilled in the art could determine the scope of the term "substituted". Moreover, Applicants have disclosed numerous specific examples of substituted aliphatic, aromatic, heteroaromatic etc. in the experimental section of the application. Applicants further submit that the definition of the term "substituted" is readily understood by one of ordinary skill in the art to include any substituent that is chemically stable when attached to the moiety that is being substituted. Applicants have discovered that irrespective of the substituents on the "substituted" moiety, the compound has the claimed utility. Therefore, Applicants' scope should not be hindered by a requirement to list all possible substituents.

The term "substituted" is widely used by those skilled in the art to describe compounds. Accordingly, recent US Patents have method claims to the use of generally "substituted" compounds. Claim 1 of US Patent No. 6,482,842 (copy attached as Exhibit 3) reads, at column 17, lines 55-58: "...and Y is optionally substituted ethylene, alkene, alkyne, or any 2 adjacent carbon atoms of a cycloalkyl or cycloheteroalkyl ring of 3-7 atoms;". Likewise, Claim 1 of US Patent No. 6,462,036 (copy attached as Exhibit 4) reads, at column 104, lines 56-63:

> X represents a) an optionally substituted group of the formula $-(CH_2)_n-$ in which n is 1, 2 or 3, b) carbonyl, c) oxygen, d) a group of the formula $-C=NOR_{10}$, in which R_{10} is a C_{1-4} alkyl group, e) a group of the formula NR_{11}, in which R_{11} is –H, an optionally substituted C_{1-4} alkyl group or an optionally substituted phenyl, of f) a group of formula $S(O)_p$ in which p is 0, 1 or 2;

Therefore, the rejection is inconsistent with current USPTO practice.

iii) With respect to the term "heterocyclic", which Applicants define as "refers to both heteroaryl groups and heterocycloalkyl groups", Applicants maintain the arguments presented in the last Reply which was filed August 26, 2002. Applicants submit that the definition of "heterocyclic" is well known and understood by one skilled in the art. A heterocyclic compound is defined as "one that contains a ring made up of more than one kind of atom" in *Organic Chemistry*, by Morrison and Boyd © 1973 Allyn and Bacon, Inc. Boston (hereinafter "Morrison and Boyd", a copy of which is attached as Exhibit A for the Examiner's convenience as Exhibit 2). As examples of heterocyclic compounds, Morrison and Boyd lists pyrrole, furan, pyridine and pyrazole, all of which Applicants list for purposes of exemplification on page 53, lines 24-26 of the instant specification. Morrison and Boyd is a widely used introductory organic chemistry textbook used at the undergraduate college level. This text is designed to teach the basic concepts of organic chemistry. The topics taught in this textbook are considered to be essential for a fundamental understanding of organic chemistry. That a definition of "heterocyclic compounds" is included in this basic organic chemistry coursebook supports Applicants' position that the term "heterocylic" is well known to one skilled in the art.

Many compounds are described as being "heterocyclic". Accordingly, recent US Patents have method claims to the use of generally "heterocyclic" compounds. Claim 3 of US Patent No. 6,482,953 (copy attached as Exhibit 5) reads, at column 26, lines 37-43

> Y is a substituent group linked to the rest of the compound by a heteroatom, the group being selected from phenoxy, 4-chlorophenoxy, 4-methylphenoxy, 4-methoxyphenoxy, 4-t-butylphenoxy, 4-t-pentylphenoxy, 2,4-di-t-butyl-phenoxy, 2,4-di-t-pentyl-phenoxy, an arylthio, an arylsulfonoyl, and a heterocyclic group.

The term "heterocyclic" is not defined within US Patent No. 6,482,953, yet the issued claims contain the term "heterocyclic". Therefore, the rejection is inconsistent with

current USPTO practice.

In addition, the 3rd Circuit Court has stated the following on the issue of knowledge of one skilled in the art and its relationship to the extent of disclosure required in a specification:

> It is axiomatic that no description, however detailed, is 'complete' in a rigorous sense. Every description will rely to some extent on the reader's knowledge of the terms, concepts, and depictions it embodies. Thus, an understanding of any description will involve some measure of inference....[S]kill in the art can be relied upon to supplement that which is disclosed as well as to interpret what is written.

Rengo Co. Ltd. v. Molins Mach. Co., 657 F.2d 535, 211 USPQ 203 (3d Cir. 1980), *cert. denied*, 454 U.S. 1055.

Applicant maintains that one skilled in the art is familiar with the above-noted terms and that the specification is fully enabling with respect to the terms objected to by the Examiner.

With regard to In re Van Guens, 988 F.2d 118, 26 PSPG2d 1057 (Ded. Cir. 1991) cited by the Examiner, Applicants are not saying that the claims are to be limited according to the definitions in the specification. Instead, Applicants are saying the term "heterocyclic" is understood by one skilled in the art.

Based upon the foregoing, the rejection of claims 1-88 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

Claims 1-88 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Altmann et al (WO 97/49706). Applicants respectfully traverse this rejection. In order for an invention to be considered obvious under 35 U.S.C. 103(a), the invention must be considered as a whole, there must be some motivation or suggestion in the prior art reference itself to modify the reference, and there must be a reasonable expectation of success.

The Court of Appeals for the Federal Circuit has stated the following on the issue of obviousness:

> Uniroyal, Inc. v. Rudkin-Wiley Corp., 837 F. 2d 1044, 1051-52, 5 USPQ 1434, 1438 (Fed. Cir. 1988), cert. denied, 109 S. Ct. 75 (1988), on remand, 13 USPQ2d 1192 (D. Conn. 1989) "Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the

> combination."; In re Stencel, 828 F. 2d 751,755, 4 USPQ2d 1071, 1073 (Fed. Cir. 1987) obviousness cannot be established "by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made."' Alco Standard Corp. v. Tennessee Valley Authority, 808 F. 2d 1490, 1498, 1 USPQ2d 1337, 1343 (Fed. Cir. 1986), cert. dismissed, 108 S. Ct. 26 (1987) "the question is not simply whether the prior art 'teaches' the particular element of the invention, but whether it would 'suggest the desirability, and thus the obviousness, of making the combination.'"; Carella v. Starlight Archery, 804 F. 2d 135,231 USPQ 644 (Fed. Cir. 1986); ACS Hospital Sys., Inc. v. Montefiore Hospital, 732 F. 2d 1572, 221 USPQ 929 (Fed. Cir. 1984) "Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so."

Donald S. Chisum, Patents, A Treatise on the Law of Patentability,, Validity and Infringement, Vol. 2, 5-218, 1992.

On page 4 of the instant Office Action, the Examiner states that "...a claim is not rejected or allowed in part but as a whole." However, the Examiner does not appear to be considering the claims as a whole, in that the Examiner has only argued that certain portions of Applicants' claim are obvious in light of Altmann. The Examiner has not shown how Altmann renders obvious the entire genus of Applications' claim. Applicants maintain that Altmann does not render claims 1-88 obivious.

In Applicants' invention, R_1 and R_2 both are more complex than R_1 and R_3, respectively, in Altmann. In addition, R_1 and R_2 can be many more possible substituents in Applicants' invention than in Altmann. None of Applicants' additional substituents are suggested by Altmann.

With respect to motivation or suggestion within the reference itself to modify the reference so that it would encompass Applicants' invention. The Examiner states on page 5 of the November 9, 2001 Office Action that:

> However, it would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole.

No such motivation or suggestion exists in Altmann. Altmann does not envisage anything other than hydrogen at the position of Applicants' R_3 group and Altmann certainly does not lead one to the complex combinations enumerated by Applicants' R_2 group. When the prior art fails to suggest the claimed invention as a whole, as it does here, any reconstruction of the prior art to obtain that invention necessarily and inevitably requires impermissible hindsight.

Applicant points out that the Court of Appeals, Federal Circuit stated in In re Grabiak that "there must be adequate support in the prior art for the ester/thioester change in structure, in order to complete the PTO's prima facie case and shift the burden of going forward to the applicant." In re Grabiak, 226 USPQ 870, 872, 1985.

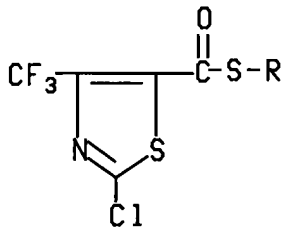
The Grabiak court further cited the following passage from In re Bergel, 292 F.2d 955, 956-57, 130 USPQ 206, 208 (CCPA 1961), in support of there ruling:

> The mere fact that it is possible to find two isolated disclosures which might be combined in such a way to produce a new compound does not necessarily render such production obvious unless the art also contain something to suggest the desirability of the proposed combination.

In re Grabiak, 226 USPQ 870, 872.

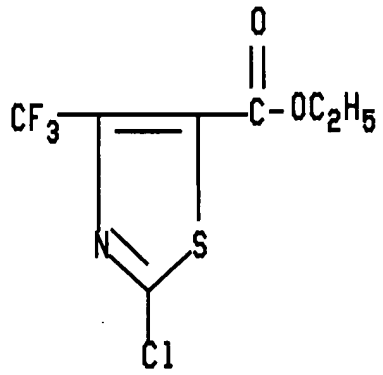
The Grabiak court made the above statement in light of the fact that both appellant's compounds and the prior art compounds were very similar in structure (see below) and had the same utility, namely, as herbicidal safeners.

Grabiak's Compound:



wherein R is C_{1-5}alkyl, phenyl or benzyl

Howe's Compound:



Note that when the R substituent is ethyl in the Grabiak compound, that the only difference in structure between Grabiak and Howe is a single atom, namely, an oxygen atom versus a sulfur atom. Hence, structural similarity and identical utility on its own cannot be the sole basis for a rejection under 35 U.S.C. § 103. Yet, the Examiner's rejection in the instant application under 35 U.S.C. § 103 does just that. The rejection is based solely upon structural and use similarity between the instant application and Altmann without any suggestion from said reference, which is in direct contravention to well-established decisions of the Court of Appeals for the Federal Circuit.

Based upon the foregoing, the rejection of claims 1-88 under 35 U.S.C. §103(a) over Altmann is obviated and should be withdrawn.

With respect to the information disclosure statement, the Examiner alleges that the information disclosure statement filed April 25, 2002 fails to comply with 37 CFR 1.98(a)(2). In a telephone call, the Examiner informed Applicants' Agent that copies of the references were not included with said information disclosure statement. As *prima facie* evidence that the information disclosure statement and copies of the references cited therein were received by the USPTO, Applicants enclose a copy of the Acknolwedgement postcard that accompanied said information disclosure statement ("Exhibit 6"). Applicants direct the Examiner's attention to the USPTO date stamp of April 25, 2002. Notwithstanding the foregoing, Applicants herewith resubmit the information disclosure statement accompanied by copies of all references cited therein. Because the information disclosure statement was originally submitted prior to the first Office Action, which was

mailed August 22, 2001, no fee is due for the submission of the instant information disclosure statement.

No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 1-88 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Respectfully submitted,

Date: November 26, 2002

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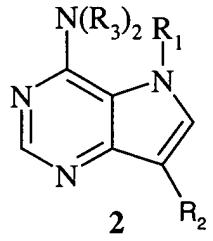
APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

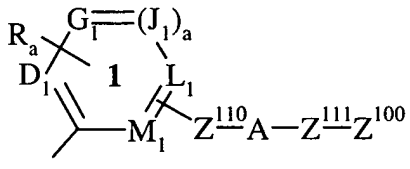
In the claims:

1. (Twice Amended) A compound of Formula (I), the racemic-diastereomeric mixtures, optical isomers[,] or pharmaceutically-acceptable salts[,] or prodrugs [or biologically active metabolites] thereof,

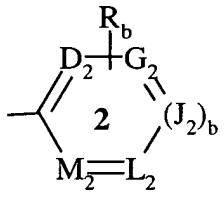


2

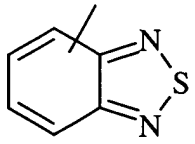
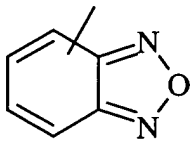
wherein:

R_1 is 

1

where Z^{100} is 

2

or a group optionally substituted with R_b selected from the group consisting of cycloalkyl, naphthyl, tetrahydronaphthyl, benzothienyl, furanyl, thienyl, benzoxazolyl, benzothiazolyl,  ,  , thiazolyl, benzofuranyl, 2,3-dihydrobenzofuranyl, indolyl, isoxazolyl, tetrahydropyranyl, tetrahydrofuranyl, piperidinyl, pyrazolyl, pyrrolyl, oxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, indolinyl, indazolyl,

benzoisothiazolyl, pyrido-oxazolyl, pyrido-thiazolyl, pyrimido-oxazolyl, pyrimido-thiazolyl and benzimidazolyl;

Z^{110} is a covalent bond, or an optionally substituted (C_1-C_6) which is optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

Z^{111} is a covalent bond, an optionally substituted (C_1-C_6) or an optionally substituted

-$(CH_2)_n$-cycloalkyl-$(CH_2)_n$-; where the optionally substituted groups are optionally substituted with one or more substituents selected from the group consisting of alkyl, CN, OH, halogen, NO_2, COOH, substituted or unsubstituted amino and substituted or unsubstituted phenyl;

R_a and R_1 each represent one or more substituents for each occurrence independently selected from the group consisting of hydrogen, halogen, -CN, -NO_2, -C(O)OH, -C(O)H, -OH, -C(O)O-alkyl, substituted or unsubstituted carboxamido, tetrazolyl, trifluoromethylcarbonylamino, trifluoromethylsulfonamido, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryl, substituted or unsubstituted alkenyl, substituted or unsubstituted aryloxy, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted arylalkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkyl, substituted or unsubstituted amido groups, substituted or unsubstituted heteroarylthio, substituted or unsubstituted arylthio, -Z^{105}-C(O)N$(R)_2$, -Z^{105}-N(R)-C(O)-Z^{200}, -Z^{105}-N(R)-S$(O)_2$-Z^{200}, -Z^{105}-N(R)-C(O)-N(R)-Z^{200}, R_c and CH_2OR_c;

where R_c for each occurrence is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, -CH_2-NR_dR_e, -W-$(CH_2)_t$-NR_dR_e, -W-$(CH_2)_t$-Oalkyl, -W-$(CH_2)_t$-S-alkyl, or -W-$(CH_2)_t$-OH;

Z^{105} for each occurrence is independently a covalent bond or (C_1-C_6);

Z^{200} for each occurrence is independently a substituted or unsubstituted (C_1-C_6), substituted or unsubstituted phenyl or substituted or unsubstituted -(C_1-C_6)-phenyl;

R_d and R_e for each occurrence are independently H, alkyl, alkanoyl or SO_2-alkyl; or R_d, R_e and the nitrogen atom to which they are attached together form a five- or six-membered heterocyclic ring; t for each occurrence is independently an integer from 2 to 6; W for each occurrence is independently a direct bond or O, S, S(O), $S(O)_2$, or NR_f, wherein R_f for each occurrence is independently H or alkyl;

or R_1 is a substituted or unsubstituted carbocyclic or heterocyclic ring fused with ring 2;

R_3 is hydrogen, hydroxy, substituted or unsubstituted alkyl or substituted or unsubstituted alkoxy;

A is -O-; -S-; -$S(O)_p$-; -N(R)-; -N(C(O)OR)-; -N(C(O)R)-; -$N(SO_2R)$-; -CH_2O-; -CH_2S-; -$CH_2N(R)$-; -CH(NR)-; -$CH_2N(C(O)R)$)-; -$CH_2N(C(O)OR)$-; -$CH_2N(SO_2R)$-; -CH(NHR)-; -CH(NHC(O)R)-; -$CH(NHSO_2R)$-; -CH(NHC(O)OR)-; -CH(OC(O)R)-; -CH(OC(O)NHR); -CH=CH-; -C(=NOR)-; -C(O)-; -CH(OR)-; -C(O)N(R)-; -N(R)C(O)-; -$N(R)S(O)_p$-; -OC(O)N(R)-; ; -N(R)-C(O)-$(CH_2)_n$-N(R)-, -N(R)C(O)O-; -$N(R)$-$(CH_2)_{n+1}$-C(O)-, -$S(O)_pN(R)$-; -O-$(CR_2)_{n+1}$-C(O)-, -O-$(CR_2)_{n+1}$-O-, -$N(C(O)R)S(O)_p$-; -$N(R)S(O)_pN(R)$-; -N(R)-C(O)-$(CH_2)_n$-O-, -C(O)N(R)C(O)-; -$S(O)_pN(R)C(O)$-; -$OS(O)_pN(R)$-; -$N(R)S(O)_pO$-; -$N(R)S(O)_pC(O)$-; -$SO_pN(C(O)R)$-; -$N(R)SO_pN(R)$-; -C(O)O-; -$N(R)P(OR_g)O$-; -$N(R)P(OR_g)$-; -$N(R)P(O)(OR_g)O$-; -$N(R)P(O)(OR_g)$-; -$N(C(O)R)P(OR_g)O$-; -$N(C(O)R)P(OR_g)$-; -$N(C(O)R)P(O)(OR_g)O$-, or -$N(C(O)R)P(OR_g)$-;

where R for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl or substituted or unsubstituted aryl;

R_g for each occurrence is independently H, substituted or unsubstituted alkyl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl or substituted or unsubstituted aryl;

p is 1 or 2;

or in a phosphorus containing group, the nitrogen atom, the phosphorus atom, R and R_g together form a five- or six-membered heterocyclic ring; or

A is $NRSO_2$ and R, R_a and the nitrogen atom together form a substituted or unsubstituted five or-six-membered heterocyclic ring fused to ring 1;

R_2 is $-Z^{101}-Z^{102}$;

Z^{101} is a covalent bond, $-(C_1-C_6)-$, $-(C_1-C_6)-O-$, $-(C_1-C_6)-C(O)-$, $-(C_1-C_6)-C(O)O-$, $-(C_1-C_6)-C(O)-NH-$, $-(C_1-C_6)-C(O)-N((C_1-C_6))-$ or a substituted or unsubstituted phenyl group;

Z^{102} is hydrogen, a substituted or unsubstituted alkyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted, saturated or unsaturated heterocyclic group, or a substituted or unsubstituted, saturated or unsaturated heterobicyclic group;

said substituted heterocyclic or substituted heterobicyclic group having one or more substituents each independently selected from the group consisting of hydroxyl, cyano, substituted or unsubstituted alkoxy, substituted or unsubstituted sulfonamido, substituted or unsubstituted ureido, substituted or unsubstituted carboxamido; substituted or unsubstituted amino, oxo, a saturated, unsaturated or aromatic, substituted or unsubstituted heterocyclic group comprising one or more nitrogen atoms, one or more oxygen atoms or a combination thereof;

wherein said nitrogen atoms are independently optionally substituted by a substituted or unsubstituted alkyl, substituted or unsubstituted aryl or substituted or unsubstituted arylalkyl group; or

R_2 is of the formula B-E, wherein B is a substituted or unsubstituted cycloalkyl,

substituted or unsubstituted azacycloalkyl, substituted or unsubstituted amino, substituted or unsubstituted aminoalkylsulfonyl, substituted or unsubstituted alkoxyalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aminoalklylcarbonyl, hydroxy, substituted or unsubstituted alkylene, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylenecarbonyl or substituted or unsubstituted aminoalkylcarbonyl group; and E is substituted or unsubstituted azacycloalkyl, substituted or unsubstituted azacycloalkylcarbonyl, substituted or unsubstituted azacycloalkylsulfonyl, substituted or unsubstituted azacycloalkylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylcarbonyl, substituted or unsubstituted heteroarylsulfonyl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted azacycloalkylcarbonylamino, substituted or unsubstituted heteroarylcarbonylamino or substituted or unsubstituted aryl;

a is 1 and D_1, G_1, J_1, L_1 and M_1 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_1, G_1, J_1, L_1 and M_1 are CR_a; or

a is 0, and one of D_1, G_1, L_1 and M_1 is NR_a, one of D_1, G_1, L_1 and M_1 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above;

b is 1 and D_2, G_2, J_2, L_2 and M_2 are each independently selected from the group consisting of CR_a and N, provided that at least two of D_2, G_2, J_2, L_2 and M_2 are CR_a; or

b is 0, and one of D_2, G_2, L_2 and M_2 is NR_a, one of D_2, G_2, L_2 and M_2 is CR_a and the remainder are independently selected from the group consisting of CR_a and N, wherein R_a is as defined above; and

n for each occurrence is independently an integer from 0 to 6.

34. A method of inhibiting one or more protein kinase activity in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolites] thereof to said patient.

35. (Amended) A method of affecting hyperproliferative disorders in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolites] thereof to said patient.

37. (Amended) A method of affecting angiogenesis in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolites] thereof to said patient.

38. (Amended) A method of treating one or more ulcers in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolites] thereof to said patient.

40. (Amended) A method of treating a condition in a patient comprising administering a therapeutically effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolites] thereof to said patient, wherein said condition is an ocular condition, a cardiovascular condition, a cancer, Crow-Fukase (POEMS) syndrome, a diabetic condition, sickle cell anaemia, chronic inflammation, systemic lupus, glomerulonephritis, synovitis, inflammatory bowel disease, Crohn's disease, glomerulonephritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, graft rejection, Lyme disease, sepsis, von Hippel Lindau disease, pemphigoid, psoriasis, Paget's disease, polycystic kidney disease, fibrosis, sarcoidosis, cirrhosis, thyroiditis, hyperviscosity syndrome, Osler-Weber-Rendu disease, chronic occlusive pulmonary disease, asthma or edema following burns, trauma, radiation, stroke, hypoxia, ischemia, ovarian hyperstimulation syndrome, preeclampsia, menometrorrhagia, endometriosis, or infection by Herpes simplex, Herpes Zoster, human immunodeficiency virus, parapoxvirus, protozoa or toxoplasmosis.

45. (Amended) A method of decreasing fertility in a patient, said method comprising the step of administering to the patient an effective amount of a compound of Claim 1 or a physiologically acceptable salt[,] or prodrug [or biologically active metabolite] thereof.

46. (Amended) The method of Claim 36 wherein the compound or a physiologically acceptable salt[,] or prodrug [or biologically active metabolite] thereof is administered in an amount effective to promote angiogenesis or vasculogenesis.

48. (Amended) The method of Claim 46 wherein the compound of Formula I, or physiologically acceptable salt[,] or prodrug [or biologically active metabolite] thereof, is administered in combination with a pro-angiogenic growth factor.